REMARKS

Claims 1-21, 23-25, and 29 of the present application are currently pending. In the Final Office Action dated December 3, 2002, claims 1-21, 23-25, and 29 have been rejected, and claim 13 has been objected to.

The cited references have been reviewed and the rejections and objection made to the claims by the Examiner have been considered. Claim 13 of the present application has been amended. For the reason set forth below, it is submitted that all claims are in condition for allowance and allowance of the application is respectfully requested.

CLAIM OBJECTIONS

In the Final Office Action dated December 3, 2003, the Examiner objected to claim 13 as containing an informality therein.

In response, the Applicants have amended claim 13. As a result, the Applicants respectfully submit that the pending claims are in condition for allowance and allowance of the claims is respectfully requested. The Applicants note that such amendments are not intended to limit the claimed invention. Rather, such amendments are being made solely in response to the Examiner's objection.

Rejections under 35 USC§112

In the Final Office Action, claim 13 was rejected under 35 U.S.C.§112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention.

In response, the Applicants have amended claim 13 of the present application. As a result, the Applicants respectfully submit that the claims as presented in the amendment conform to all applicable requirements under 35 U.S.C.§112 and that the rejection be withdrawn.

REJECTIONS UNDER 35 USC §103(A)

In Final Office Action dated December 3, 2002, claims 1-21, 23-25, and 29 were rejected under 35 USC § 103(a) as being unpatentable over United States Patent No.

5,641,510, issued to Clark et al. (herein after "Clark") in view of the article entitled "Evaluation of Sodium colistimethate Aerosol," authored by Rose et al. (Hereinafter "Rose") in further view of the article entitled "A re-assessment of in-vitro activity of Colistin SMS," authored by Catchpole et al. (hereinafter "Catchpole"). For the reasons set forth below, the Applicants respectfully traverse the Examiner's rejections and respectfully request allowance of the application.

To establish a prima facie case of obviousness, three basic criteria must be met by the Examiner. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. (see MPEP §2143.03).

Claim 1 of the present application is directed to micronized powder particles of colistin sulphomethate sodium wherein at least 90% by volume of the micronized particles have a diameter of from 0.01 to 10 micrometers for use in the treatment of a pulmonary infection by powder inhalation, wherein the colistin sulphomethate sodium is not separated into component form.

Similarly, claim 15 of the present application pertains to a capsule containing micronized colistin sulphomethate sodium wherein at least 90% by volume of the micronized powdered particles have a diameter of from 0.01 to 10 micrometers.

The Clark reference is directed to a method for treating capsules used for drug storage and includes exposing a lubricant-coated inner surface of the capsule to a solvent which is different from the lubricant, wherein the solvent dissolves the lubricant but not the capsule, and inserting a pharmaceutical powder into the capsule. In another embodiment, the Clark reference is directed to a method of treating a capsule for storing pharmaceutical powder which is administered to the patient as an aerosol, the capsule having a mould-releasing lubricant and includes dusting the lubricant-coating inner surface of the capsule with a pharmaceutically acceptable dusting agent which is different from the pharmaceutical powder and has an average particle size of between

0.1 to 2.0 micrometers, wherein the dusting agent absorbs the lubricant, and inserting the pharmaceutical powder in the capsule. The Clark reference fails to teach or suggest administering micronizied powder particles of colistin sulphomethate sodium for use in the treatment of a pulmonary infection by powder inhalation.

The Rose reference discloses an evaluation of sodium colistimethate aerosol in gram-negative infections of the respiratory tract. More particularly, the Rose reference discloses using sodium colistimethate (CSM) dissolved in sterile water to obtain an aerosol having a concentration of 50 mg/ml. The CSM aerosol was then administered with the use of an intermittent positive-pressure breathing instrument to yielding a particle size of 1-7 microns. The aerosol administered to patients was shown to be effective in eradicating or suppressing susceptible gram-negative organisms carried in the respiratory tract of patients with underlying pulmonary disease. In the Rose reference CSM was dissolved in sterile water to form an aerosol prior to administering the drug to a patient. As such, the CSM aerosol disclosed in Rose is not a micronized powder. Therefore, Rose fails to teach or suggest administering micronizied powder particles of colistin sulphomethate sodium for use in the treatment of a pulmonary infection by powder inhalation.

The Catchpole reference discloses a reassessment of the in-vitro activity of collistin sulphomethate sodium. More specifically, Catchpole examines the use of collistin sulphomethate sodium in treating gram-negative bacteria. In the Catchpole experiment, 377 clinical isolates, NCTC control organisms, and organisms with known mechanisms of resistance were subjected to collistin sulphomethate sodium. MICs were determined using an agar dilution technique. IsoSensitest agar was inoculated with bacteria to give a final inoculum of 10^4 CFU. In the disclosure, Clark fails to contemplate any method of delivering collistin sulphomethate sodium to a patient. As such, the Catchpole reference fails to teach or suggest administering micronizied powder particles of colistin sulphomethate sodium for use in the treatment of a pulmonary infection by powder inhalation.

Moreover, the Applicants respectfully submit that the Examiner has failed to establish a prima facie case of obviousness. As stated above, three basic criteria must

be met by the Examiner failed to establish a prima facie case of obviousness. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. The Applicants respectfully submit that no such suggest or motivation to combine the references has been exhibited thus far by the Examiner. Rather, the Applicants respectfully submit that the Examiner has used impermissible hindsight to recreate the Applicant's disclosure.

Second, there must be a reasonable expectation of success. The Applicants respectfully submit that a person of ordinary skill in the art would not have a reasonable expectation of success when combining the teachings of Clark, Catchpole, and Rose. Clark does not teach or suggest that the drugs disclosed therein may be readily substituted with colistin SMS. That is, those skilled in the art appreciate that colistin SMS has vastly different drug loading characteristics as compared to the drugs disclosed in Clark. More specifically, colistin SMS a very high loading of drug is required (approximately 125 milligrams) whereas the drugs disclosed in Clark (See Table 2) are delivered in sub-milligram quantities. As a result, the amount of collistin SMS powder which would be retained in the capsule is a very low percentage, due to the very high amount of powder which is in the capsule itself. Therefore, Clark can only be seen as being a general description of the use of micronized powders in inhalation therapy with no description (either in general of specific terms) to Colistin SMS.

Additionally, taking the disclosure of Clark, Catchpole and Rose in combination, one of ordinary skill in the art would not arrive at the subject matter of the present invention. The teaching of Rose indicate the use of liquid aerosol administration of colistin SMS, while Catchpole failed to contemplate any delivery mechanism whatsoever. The Applicants have found that colistin SMS may be delivered in a micronized dry powder form. This is clearly not taught in the prior art references cited by the Examiner. There is no indication to one of ordinary skill in the art that the composition of Clark could be substituted by colistin SMS as taught by Rose and Catchpole.

Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. (see MPEP §2143.03). The Applicants respectfully submit that the cited prior art references fail to teach or suggest all the claim limitations. More specifically, neither Clark, Rose nor Catchpole teach micronized powder particles of colistin SMS. Rather, Clark teaches that pharmaceutical powders may be included within a capsule treated with a lubricant. Rose teaches diluting colistin SMS in sterile water prior administering the material to a patient as a liquid aerosol. As such, the Rose reference teaches away from administering colistin SMS to a patient in powder form as disclosed in the present application. The Clark reference fails to teach or suggest any delivery mechanism for colliston SMS.

Accordingly, Applicants respectfully submit that the claims of the present invention are patentable over the cited prior art references and request allowance of the presently pending claims.

CONCLUSION

In view of the above remarks and amendments, it is submitted that the pending claims are in condition for allowance and their allowance is earnestly solicited.

If any issues remain, the Examiner is urged to contact the undersigned by telephone for a prompt resolution thereof.

No additional fees are seen as being necessary in connection for this amendment. However, the Examiner is authorized to charge any additional fees or credit any overpayment to Deposit Account 50-1329.

Respectfully submitted,

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